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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/363,748	07/30/1999	CAROL WATKINS	108137.701	8501

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EXAMINER	
CRANE, LAWRENCE E	
ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 06/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/363,748	WATKINS ET AL.	
	Examiner	Art Unit	
	L. E. Crane	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *February 9, 2004 (amdt/Declaration)*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *39,43,44,46-49 and 51-53* is/are pending in the application.

4a) Of the above claim(s) *51-53* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *39,43,44 and 46-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *02/20/2004*.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

No additional claims have been cancelled, claim **39** has been amended, the disclosure has not been further amended, and new claims **51-53** have been added as per the amendment filed February 9, 2004. The Information Disclosure Statement (IDS) filed February 9, 2004 with all cited references has been reviewed and made of record.

Claims **39, 43-44, 46-49 and 51-53** remain in the case.

Newly submitted claims **51-53** are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: no originally filed claim has been directed to the effect of uridine phosphate administration in gerbils on the levels of uridine and cytidine in the gerbil nervous system and therefore this effect has not been the subject of a literature search.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims **51-53** are withdrawn from consideration as being directed to a non-elected invention. See 37 C.F.R. §1.142(b) and MPEP §821.03.

Claims **39, 43-44 and 46-49** remain under examination in the case.

This application has been filed with informal drawings which are acceptable for examination purposes only. Formal drawings will be required when the application is allowed.

Examiner notes the submission of a second declaration filed under 37 C.F.R. § 1.132 by applicant Wurtman. The declaration explains the meaning inherent in Figure 4 originally filed with the instant application as showing increases in the levels of both cytidine and uridine levels in the gerbil brain following administration of uridine nucleotides by ingestion. The gerbil brain is also asserted to be a closer analogue to the human brain based on prior art reports (references kindly supplied) that the steady state levels of both cytidine and uridine are nearly identical in both species. The declaration then asserts that because of the measurements shown in Figure 4 must be seen as a basis for understanding that the instant claimed method does improve memory

performance in humans. Examiner further responds to the substance of applicant Wurtman's declaration as appropriate in the rejections below.

Claims **39, 43-44 and 46-49** are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Inspection of the instant disclosure reveals no specific test data to support the generic limitation "enhancing memory" directed to the treatment of a disease condition or conditions, by the administration of any "uridine phosphate." For example, the noted claims read on the treatment of senile dementia, HIV-related dementia, and Alzheimer's disease, but the instant disclosure fails to provide any evidence that the instant method is effective in the treatment of any one of these disease conditions in any mammalian host. Therefore, the instant disclosed exemplifications relevant to the instant claims are deemed to be entirely prospective and therefore lacking any enabling effect.

Applicant's arguments and declaration filed February 9, 2004 have been fully considered but they are not persuasive.

Applicant has only shown and provided an enabling disclosure in support of the finding that gerbils reveal an increase in the concentrations of uridine and cytidine in a portion of the gerbil nervous system following administration of a uridine phosphate orally. However, this subject matter has not been previously claimed and therefore not searched. Therefore, in light of the withdrawal of claims **51-53**, the newly claimed subject matter cannot be considered herein.

The following is a quotation of 35 U.S.C. §103(**a**) which forms the basis for all obviousness rejections set forth in this Office action:

> "A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made."

Claims **39 and 43-44** are rejected under 35 U.S.C. §103(**a**) as being unpatentable over **Rüthrich et al.** (PTO-892 ref. **UA**) in view of **Polifarma '267** (PTO-892 ref. **L**) and **Piazza et al. '459** (PTO-892 ref. **B**) and further in view of applicant's own admissions.

The instant claims are directed to enhancement of memory by administration to a host in need thereof an effective amount of a "uridine phosphate" which term applicant defines as 5'-UMP, 5'-DMP or 5'-UTP.

Applicant is referred to the abstract of **Rüthrich et al.** which teaches that the administration of uridine is correlated with enhanced memory retention in rats.

Applicant is referred to claim ***6*** of the **'267** reference which is directed to pharmaceutical compositions including " ... an amount of uridine therapeutically effective in reducing deficits in neuronal functional activity ... ." Whether this is accomplished by increasing cytidine levels in the brain or is otherwise directly effective is deemed to be impossible to determine.

Applicant is referred to claim ***1*** in the **'459** reference wherein the subject matter claimed includes "treatment of disturbances of the nervous system ... " by "administering ... an effective amount of uridine ... ." Applicant is also referred to column 9, line 58 through column 10, line 4 of the **'459** patent wherein the oral administration of uridine is specifically disclosed along with the teaching that oral administration had the potential to be as effective as Nerve Growth Factor (NGF) in the treatment of numerous "invalidating diseases" including "pathological aging."

Applicant's admission at paragraph "3" of the declaration filed September 22, 2003 includes the statement that "[u]ridine is phosphorylated by ubiquitous pyrimidine nucleoside kinase enzymes ("uridine kinase") to form uridine monophosphate (UMP). These enzymes attach the phosphate moiety to the 5-prime hydroxyl on the ribose ring of the uridine molecule. UMP can be further phosphorylated to form uridine 5-prime di-phosphate (UDP) by the enzyme(s) pyrimidine nucleoside monophosphate kinase. UDP can be converted to uridine 5-prime tri-phosphate (UTP) by the nucleoside diphosphokinase enzymes(s)." Additionally, in paragraph 3 of the Wurtman declaration of February 9, 2004, Prof. Wurtman, referring to the results summarized in Figure 4, states that "these results are also representative of uridine mono-phosphate

(UMP) administration, because UMP is quantitatively hydrolyzed to uridine by enzymes in the intestinal mucosa before entering the blood." Therefore, the treatment of a human host with uridine is, by applicant's own admission, well known in the art to be entirely equivalent to treatment of the same host with any one of 5'-UMP, 5'-UDP or 5'-UTP or a mixture thereof.

One of ordinary skill would have been motivated to combine the instant references because each disclosure is directed to the administration of UMP or uridine or a compound which generates uridine in vivo for the purpose of effecting an increase in the concentration of uridine in the nervous system of a mammalian host. Applicant's admissions are combined as well to insure that the knowledge of the ordinary practitioner concerning the interconversions of uridine phosphates and uridine known to occur in vivo are provided to make clear the significance of the prior art reference subject matter when compared with the instant claimed subject matter.

It would have been obvious to the ordinary practitioner to conclude, in light of applicant's own admissions of what is notoriously well known in the art, that the administration of UMP as taught by **Rüthrich et al.** or the administration of uridine as taught by either of **Polifarma '267** and by **Piazza et al. '459** would produce the same effect as the administration of a mixture of uridine 5'-mono-, 5'-di- and 5'-tri-phosphates orally and would be expected to have the same effect as that claimed herein.

Therefore, the instant claimed method of memory enhancement would have been obvious to one of ordinary skill in the art having the above cited reference before him at the time the invention was made.

Applicant's arguments filed February 9, 2004 have been fully considered but they are not deemed to be persuasive.

Applicant's arguments and declaration filed February 9, 2004 have been fully considered but they are not persuasive.

Claims **39 and 44** are rejected under 35 U.S.C. §103(**a**) as being unpatentable over **Merlini et al.** (PTO-892 ref. **T**) in view of applicant's own admission at paragraph "3" of the declaration filed September 22, 2003 and applicant's admissions at paragraph 3 of the declaration filed February 9, 2004.

The instant claims are directed to enhancement of memory by administration to a host in need thereof an effective amount of a "uridine phosphate" which term applicant defines as 5'-UMP, 5'-DMP or 5'-UTP.

Applicant is referred to the abstract supplied, which teaches that administration of uridine is effective in improving several mental functions including "memorisation." Whether this is accomplished by increasing cytidine levels in the brain or is otherwise directly effective is deemed to be impossible to determine.

Applicant's admission at paragraph "3" of the declaration filed September 22, 2003 includes the statement that "u]ridine is phosphorylated by ubiquitous pyrimidine nucleoside kinase enzymes ("uridine kinase") to form uridine monophosphate (UMP). These enzymes attach the phosphate moiety to the 5-prime hydroxyl on the ribose ring of the uridine molecule. UMP can be further phosphorylated to form uridine 5-prime di-phosphate (UDP) by the enzyme(s) pyrimidine nucleoside monophosphate kinase. UDP can be converted to uridine 5-prime tri-phosphate (UTP) by the nucleoside diphosphokinase enzymes(s)." Additionally, in paragraph 3 of the Wurtman declaration of February 9, 2004, Prof. Wurtman, referring to the results summarized in Figure 4, states that "these results are also representative of uridine mono-phosphate (UMP) administration, because UMP is quantitatively hydrolyzed to uridine by enzymes in the intestinal mucosa before entering the blood." Therefore, the treatment of a human host with uridine is, by applicant's own admission, well known in the art to be entirely equivalent to treatment of the same host with any one of 5'-UMP, 5'-UDP or 5'-UTP or a mixture thereof.

It would have been obvious to the ordinary practitioner to conclude, in light of applicant's own admissions of what is notoriously well known in the art, that the administration of uridine as taught by **Merlini et al.** would be in effect the administration of a mixture of uridine 5'-mono-, 5'-di- and 5'-tri-phosphates and would be expected to have the same effect as that claimed herein.

Therefore, the instant claimed method of memory enhancement would have been obvious to one of ordinary skill in the art having the above cited reference before him at the time the invention was made.

Applicant's arguments and declaration filed February 9, 2004 have been fully considered but they are not persuasive.

The above grounds of rejection have been amended to exclude claim **43** wherein the co-administration of cytidine is specifically excluded. Otherwise the instant grounds of rejection are deemed to remain valid and therefore have been maintained.

Applicant's amendment necessitated the new grounds of rejection. Accordingly, **THIS ACTION IS MADE FINAL**. Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. §1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. §1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

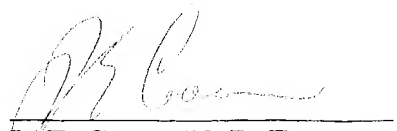
Papers related to this application may be submitted to Group 1600 via facsimile transmission (FAX). The transmission of such papers must conform with the notice published in the Official Gazette (1096 OG 30, November 15, 1989). The telephone number to FAX (unofficially) directly to Examiner's computer is 571-273-0651. The telephone number for sending an Official FAX to the PTO is 703-872-9306.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner L. E. Crane whose telephone number is **571-272-0651**. The examiner can normally be reached between 9:30 AM and 5:00 PM, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson, can be reached at **571-272-0661**.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is **571-272-1600**.

LECrane:lec
06/14/2004



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